

# Wernicke–Korsakoff syndrome in a patient with self-neglect associated with severe depression

Karen A Cocksedge<sup>1</sup> and Adrian Flynn<sup>2</sup>

<sup>1</sup>Carrick North Community Mental Health Team, 57 Pydar Street, Truro, Cornwall TR1 2SS, UK

<sup>2</sup>Psychiatric Liaison Service, Wellbeing Centre, Royal Cornwall Hospital, Truro, Cornwall TR1 3LJ, UK

**Corresponding author:** Karen A Cocksedge. Email: karen.cocksedge@doctors.org.uk

## Lesson

Wernicke–Korsakoff syndrome is a neuropsychiatric disorder resulting from thiamine deficiency and commonly associated with chronic alcoholism, but we describe the first case report resulting from self-neglect associated with depression.

## Keywords

nutrition and metabolism, psychiatry, Wernicke–Korsakoff syndrome, thiamine deficiency, depression, weight loss

## Case report

The patient is a 68-year-old gentleman who was diagnosed in April 2011 with a high-grade lymphoma. In the month prior to diagnosis, he experienced 13 kg of weight loss; after diagnosis, he developed a severe depression with extreme loss of appetite and proceeded to lose a further 23 kg over the following four months (body mass index reduced to 14.5). He was treated with chemotherapy between April and August 2011 and showed a good partial response to treatment. In August, three weeks after his last chemotherapy, he was admitted with a three-day history of confusion. He was found to be severely hypoglycaemic (1.9 mmol/L) and was treated with infusions of 50 ml 10% glucose until normoglycaemic. There was no history of alcohol use and his blood results did not suggest chronic alcoholism. A septic screen showed a slight leucocytosis ( $11.9 \times 10^9/L$ ) with neutrophilia ( $10.9 \times 10^9/L$ ), but chest X-ray, mid-stream urine, blood cultures and stool cultures were all normal. A head computed tomography showed no acute changes and no cerebral lymphoma. Over the next four days, he received repeat intravenous infusions of 5% dextrose without thiamine, nutritional supplements were started and he was also given co-amoxiclav in case of undetected infection. During this time, he showed good improvement, maintaining normoglycaemia whilst his neutrophilia and confusion resolved. However, on day 6 of admission, he deteriorated again with a new onset of

confusion, this time accompanied by ataxia, agitation and visual hallucinations. Over the next three days, he became increasingly withdrawn and progressively drowsy, with episodes of hypothermia. This time he remained normoglycaemic and a repeat septic screen was negative. The only blood results of significance were hypomagnesaemia (0.34 mmol/L), but intravenous replacement of magnesium did not improve his condition, and a slightly low folate (3.5 ng/mL) for which folic acid was commenced. At this time, consideration was given to the possibility of Wernicke's encephalopathy and intravenous thiamine was prescribed, with an initial dose of 500 mg, then 250 mg twice daily for three days. Under dietetic guidance, nasogastric feeding was commenced at a slow initial rate and we prescribed 15 mg mirtazapine for depression. In the days that followed, his confusion improved, but he became apathetic and by day 21, there was evidence of short-term memory loss. Thiamine was re-started (300 mg/day, orally) and by discharge, over three weeks later, confusion, apathy and short-term memory deficits had all resolved. His depression also improved significantly, which we attribute to a combination of mirtazapine, improved nutrition and appropriate social support.

## Discussion

Wernicke's encephalopathy is a neuropsychiatric disorder resulting from acute thiamine deficiency, traditionally described as the triad of confusion, ataxia and ophthalmoplegia. However, the classical triad is only observed in a minority of cases with other possible signs including hypothermia, hypotension, tachycardia and hallucinations. With early recognition and treatment with intravenous thiamine, the condition can be reversed, but if untreated it can develop into Wernicke–Korsakoff syndrome, coma or even death. The classic signs of progression into Wernicke–Korsakoff syndrome include anterograde amnesia, often leading to confabulation, and apathy; these signs often emerge as the acute

confusional state associated with Wernicke's encephalopathy begins to resolve. Traditionally, the typical signs of Korsakoff's syndrome, once present, are regarded as irreversible.<sup>1</sup> Clinically, Wernicke–Korsakoff syndrome is usually associated with chronic alcoholism, but there is now increasing recognition that this condition can be associated with any cause of chronic low intake of thiamine or chronic malabsorption, such as in hyperemesis gravidarum, after bariatric surgery, in Crohn's disease and in AIDS, for example. In particular, there is increasing awareness of the risk of Wernicke–Korsakoff syndrome in anorexia nervosa, following several case reports<sup>2–5</sup> and a study suggesting that thiamine deficiency was present in 30% of patients hospitalized for anorexia nervosa.<sup>6</sup> Whilst there is growing evidence of the syndrome resulting from self-imposed starvation in anorexia nervosa, there is very little recognition of the risk of Wernicke–Korsakoff syndrome in other psychiatric illnesses resulting from general self-neglect.<sup>7</sup>

In this case, we believe the patient initially presented with neuroglycopenia, but after successful treatment, developed Wernicke's encephalopathy with progression into Wernicke–Korsakoff syndrome. To our knowledge, this is the first case report to associate Wernicke–Korsakoff syndrome with self-neglect resulting from severe depression. It is likely that, in addition, the patient's lymphoma and treatment with chemotherapy also contributed to his loss of appetite. Less likely differential diagnoses include severe depression with psychosis or depressive pseudodementia, but these do not explain ataxia or hypothermia; delirium from hypomagnesaemia, but magnesium treatment did not improve his condition; delirium from folate deficiency, but deficiency was only mild, was likely chronic and, in any case, does not explain hypothermia; or finally starvation induced hypercortisolism which could explain many of the symptoms including psychosis and memory impairment<sup>8</sup> but would not explain hypothermia or the acuteness of presentation.

In this case, four days of intravenous thiamine treatment quickly reversed the patient's confusion and ataxic symptoms, but after treatment was stopped, he developed apathy and short-term memory deficits typical of Korsakoff's syndrome. However, with further prolonged thiamine treatment, these symptoms also eventually resolved. There are two similar case reports in the literature which show complete recovery from an undertreated Wernicke–Korsakoff syndrome with prolonged thiamine treatment<sup>9</sup> and we believe our third case adds weight to the argument that Korsakoff's syndrome may not be as irreversible as traditionally regarded.

The rarity of Wernicke–Korsakoff syndrome associated with non-alcoholic self-neglect is likely because the non-alcoholic cases are not predisposed to the condition by the effects of alcohol on thiamine transport and utilization. In the rare non-alcoholic cases where the condition does develop, there may be a genetic predisposition such as via genes involved in cellular transport of thiamine (THTR1, THTR2).<sup>10</sup>

In summary, this case highlights the importance of considering Wernicke–Korsakoff syndrome in the context of general self-neglect in psychiatric conditions other than anorexia nervosa and also highlights the importance of continuing prolonged thiamine treatment with a view to potentially reversing the condition completely.

#### Declarations

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